

### **AMENDMENTS TO THE SPECIFICATION**

Please amend the paragraph beginning on line 13 of page 16 as follows:

FIG. 11 shows the nucleotide sequence of the accessible region located around 1,000 base pairs upstream of the transcriptional startsite of the human VEGF gene. Target sites for various transcription factors are indicated. Sequences of the murine (SEQ ID NO. 23) and human VEGFA (SEQ ID NO. 24) genes in this region are shown.

Please amend the paragraph beginning on line 13 of page 88 as follows:

The JNK family of proteins is also activated by certain growth factors, although less efficiently than the ERK family. Efficient activation of JNK proteins is induced by inflammatory cytokines and cellular stresses of a different nature that can be mediated via G-protein-coupled receptors (GPCR). Bioactive amines, peptides, glycopeptides, phospholipids, proteases, odorants, certain taste ligands and even photons can all promote the functional coupling of their receptor-ligand complex with heterotrimeric G proteins located at the intracellular side of the plasma membrane. This causes a conformational change in three key flexible “switch” regions in the G-protein alpha subunit, thereby promoting the exchange of the bound GDP for GTP and the dissociation of the  $\beta\gamma$  heterodimers (FIG. 12). In turn, GTP-bound G protein  $\alpha$ -subunits and complexes initiate a broad range of intracellular signaling events, including the activation of classic effectors such as adenylyl cyclases, phosphodiesterases and phospholipases, and the regulation of activity of ion channels, ion transporters and several protein kinases. As with tyrosine kinase receptors, GPCR are able to promote the activation of guanine nucleotides exchange factors (GEFs) acting on small GTP-binding proteins of the Ras superfamily. The Ras/Rac pathway is involved in the kinase cascade leading to JNK. Another mammalian cell mitogen-activated protein kinase (MAPK) scaffold protein, JIP-1 (JNK-interacting protein-1) has been shown to inhibit the JNK activity (FIG. 13(B)). JIP-1 also binds a to various MAPK kinases (e.g., MKKKK, MKKK and MKK) for selective regulation of JNK activation. A third potential MAPK scaffold protein in mammalian cells is a functional MKKK (FIG. 13(C)). The MAPK/ERK kinase kinase MEKK1 binds directly to JNK.